REMARKS

The Examiner has rejected claims 1, 3, 5 – 6, and 11 under 35 USC 103(a) as being unpatentable over Swan et al. (US Pat. 5 563 056) or Hubbel et al. (US 5 529 914) in view of Chai-Gao et al. (US 5 858 802). He has further rejected claims 1, 3 and 5 – 15 under 35 USC 103(a) as being unpatentable over Swan et al., or Hubbel et al. in view of Wessa et al. (WO 97/43631)

Swan et al., Hubbel et al. and Chai-Gao et al. have been previously cited by the Examiner and have been discussed in an earlier response, Wessa et al. has been newly applied by the Examiner.

Wessa et al. (WO 97/43631), which is assigned to the assignee of the present application, discloses a sensor for detecting proteins on the key-lock reaction principle consisting of a sensor body having a surface coated with a polymer layer where the receptor molecules on the key-lock reaction are bonded to the polymer layer. The bond between the polymer and the receptor molecules is provided by a photoreactive molecule which is covalent to the lysine of the receptor molecule and inserted into a C-H bond of the polyimide.

In accordance with claim 1 of the present application a dextran coating is attached to a carrier surface with a connection formed by a photo-linker by way of co-immobilization of a mixture of the dextran and a 3-trifluoromethyl-3-(m-isocyanophenyl)-diazinine (TRIMID)-modified protein as photolinker.

As the Examiner has stated Swan et al. teaches a process for the preparation of cross-linked matrices containing immobilized chemical species, the matrices being preferably formed on a substrate surface. Swan et al. teaches how, and which type of, latent reactive groups can be generated. Also, dextran is mentioned as a polymer from which the coupling compound may be derived.

However, Swan et al. does not teach how a photoactive and diazinine-functionalized dextran-analogue is prepared. The patent does not teach how the photo active diazinine-functionalized dextran analogue is activated and it does not teach, or in any way suggest, that carbenes are able to form cross-links with dextran polymers and chemical species to be immobilized.

In Swan et al. monosaccharides and dextran sulfate are explicitly named as photo derived polymers.

Hubbel et al. (US 5 529 914) discloses a completely different way of obtaining photochemical cross-links. Here, low molecular weight diffusable photo-initiators are used to generate free radicals (col. 1, lines 55-65). The radical generators, which are called photo initiators, are not chemically linked to polymers. The diffusable photo-initiators generate free radicals upon activation by light. The free radicals activate the carbon-carbon double bond in specifically synthesized macromers (col. 11, lines 8 to 15). The macromers are (ethylenically unsaturated) derivatives of PEO, PEG...dextran, ...(col 11, lines 19 – 26).

It is noted that the photoinitiator used by Hubbel et al. is a diffusable dye. Swan et al., in contrast, mentions photo-generated (acryl derived or kety radicals) intermediates which are bound to polymers. This is based on a completely different approach. Yet the Examiner uses the same terms for both processes and consequently bases his conclusion on a combination of different concepts. Not combining these Swan + Hubbell

It is certainly not correct that the teaching of Hubbel et al. suggests the possibility of using a dextran-based photolinker polymer to properly bio-engineer a biosensor platform. That is such a procedure is not obvious from the cited references. treated in present claims

The teachings of Hubbel et al. concern the formation of biocompatible membranes around biological materials, whereas Swan et al. summarize established procedures (see Gao, H. Kislig E., Oranth, N. and Sigrist, H. Photolinker polymer mediated immobilization of monoclonal antibodies, F(ab')2 and F(ab') fragments, Biotech. appl. Biochem. (1994) 20, 251-263) in view of medical device coating applications. Neither of the two patents suggests application for biosensing purposes. NOT in present claims

Chai-Gao (US 5 858 802) essentially teaches that photo generated carbenes are capable of effecting insertion reactions into co-valently bonded inorganic nitride such as silicon nitride or boron nitride (col 7, claim 1). The patent also teaches that polysaccharides, among other biomolecules and biologically active substances can be linked to co-valent nitrides.

The references cited by the Examiner do certainly not suggest the attachment of a dextran coating to a carrier by co-immobilization of a mixture of the dextran and a 3-trifluoromethyl-3-(m-isocyanophenyl)-diazinine (TRIMID)-modified protein as a photolinker. A single ↓ Yes

In column 5, line 55, Swan et al. mentions as a possible linker 3-trifluoromethyl-3-phenyl diazinine as pointed out by the Examiner. This however is a different component. And it is not seen how the photo-activator, being preferably a TRIMID-modified protein such a T-BSA, renders the use of a mixture of dextran and a 3-trifluoromethyl-3-(m-isocyanophenyl) diazinine (TRIMID) modified protein as photolinker obvious.

The Examiner has stated that, although Swan et al. and Hubbel teach coating processes, they do not teach TRIMID modification, the use of BSA or polyimide nor an application to biological sensors.

Wessa et al. teaches a process for producing a sensor for detecting proteins. The sensor consists of a body having a surface, which is coated with a polymer layer with receptor molecules bonded to the polymer layer. The bond between the polymer and the receptor molecules is provided by a photo-reactive molecule that is covalent to the lysine of a receptor molecule inserted into the polyimide and the photo-reactive molecule is preferably TRIMID. The Examiner concludes herefrom that it would have been obvious to use the TRIMID-modified photo-initiator and polyimide of Wessa et al. with the Swan et al. or Hubbel et al. methods.

It is asserted however that, for an expert in the field, it is by no means obvious to conclude that a paralene coated and with dextron bioengineered mass sensor platform can be used for the detection of biological interactions on the basis of:

1. the suggestion that photo-generated carbenes may be immobilize polysaccharides (on implant surfaces) and that

2. polysaccharides, that is, dextran after appropriate modification, can be polymerized by activation of a diffusable photo-initiator. Wessa et al. discloses covalently linked (not diffusable) carbene mediated immobilization of a biomolecule to polyimide.

Wessa et al. describes a method to directly functionalize an enzyme with a photo-activatable hetero-bifunctional cross-linker (that is, attaching the photo-active reagent at the probe molecule) and bio-detection after surface immobilization of such modified probe molecules on surface acoustic platforms.

On the basis of the above comments it is asserted that the present invention as defined in claim 1 is not rendered obvious by any combination of the cited references.

Reconsideration of claim 1 and together therewith of the dependent claims 3 and 5 to 15 is respectfully requested and allowance of these claims is solicited.

Respectfully submitted,

K. Bach

Klaus J. Bach, Reg. No. 26832